IN THE UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF MISSOURI
EASTERN DIVISION

B.F., a minor, BETH FORBES, individually and as next friend of B.F., and THOMAS FORBES, individually and as next friend of B.F.,	)	Case No. 4:12-cv-01760-CAS
Plaintiffs,	)	
v.	)	JURY TRIAL DEMANDED
ABBOTT LABORATORIES INC., et al.,	)	
Defendants.	)	

DEFENDANT ABBOTT LABORATORIES INC.'S
OPPOSITION TO PLAINTIFFS' MOTION *IN LIMINE* NO. 6

Defendant Abbott Laboratories Inc. submits this memorandum in opposition to plaintiffs' motion *in limine* no. 6 to exclude all evidence, testimony, and argument from Dr. Christopher B. Ticknor ("Dr. Ticknor") regarding the adequacy of Depakote's warnings or its risk of birth defects.

INTRODUCTION

Plaintiffs' motion to exclude Dr. Ticknor's opinions regarding the adequacy of Depakote's warnings and Depakote's risk of birth defects is an untimely *Daubert* motion, and should be denied for that reason alone. Even if timely, the motion is unsupportable, both legally and factually. Legally, missing from plaintiffs' motion is any authority – from this Court or others within the Eighth Circuit – that supports their arguments.[1] Factually, plaintiffs ignore

[1] Throughout the entire argument section of their motion, plaintiffs cite just one case from the Tenth Circuit, *Ralston v. Smith & Nephew Richards, Inc.*, 275 F.3d 965 (10th Cir. 2001). (*See* pls.' memo. at 7, Doc. 151.) Plaintiffs' reliance on that case is misplaced given that Dr. Ticknor's qualifications to opine on Depakote's warnings and birth defect risk – unlike those of

numerous details about Dr. Ticknor's medical knowledge, training, and experience that qualify him to opine on Depakote's warnings and risk of birth defects. As set forth in detail below, plaintiffs' motion should be denied.

ARGUMENT

I. Plaintiffs' Motion Should be Denied Because it is an Untimely *Daubert* Motion

Under this Court's Third Amended Case Management Order, motions to exclude testimony pursuant to *Daubert v. Merrell Dow Pharm., Inc.,* 509 U.S. 579 (1993) were due September 2, 2015. (Doc. 50 at 1.) Plaintiffs did not file any *Daubert* motions by that date. Instead, they have tried to skirt the applicable filing deadline, as well as the requisite *Daubert* showings, by styling the present motion as a "motion *in limine*." Despite their efforts, there is no doubt that plaintiffs' motion is a *Daubert* motion because it attacks Dr. Ticknor's opinions based on qualifications and relevance. *See American Auto Ins. Co. v. Omega Flex. Inc.*, 783 F.3d 720, 722-23 (8th Cir. 2015) (noting that under the "*Daubert* inquiry" the trial judge has to determine whether the proffered expert has "sufficient specialized knowledge to assist the jurors in deciding the particular issues in the case"); *Pestel v. Vermeer Mfg. Co.*, 64 F.3d 382, 384 (8th Cir. 1995) (noting that under *Daubert* "it is the trial judge's duty to screen [expert opinion] evidence for relevance and reliability"). The Court should therefore deny the motion because it is untimely. *See e.g., Bartell v. Govoreau*, No. 04-0391-CV-W-FJG, 2005 WL 5989792, *3 (W.D. Mo. Sept. 23, 2005) (finding the motion to exclude testimony of an expert untimely because the court's scheduling order clearly stated the deadline for *Daubert* motions had passed).

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the expert in *Ralston* – are based on more than the single fact that he is a physician, as explained in more detail herein.

II. Dr. Ticknor's Qualifications

Dr. Ticknor is a physician licensed to practice medicine in Texas.[2] As a psychiatrist, he specializes in the area of mental health and mental illnesses, with an emphasis on the study and treatment of mood disorders such as bipolar disorder, depression, and anxiety.[3] Dr. Ticknor is board certified in psychiatry by the American Board of Psychiatry and has served as a Part II Oral Examiner for the American Board of Psychiatry and Neurology in past years.[4] He holds an appointment as an Associate Adjunct Professor of Psychiatry at the University of Texas Health Center in San Antonio, where he completed his residency training in 1986 and served one year as Chief Resident in the department.[5] Dr. Ticknor has remained on the clinical faculty of the University of Texas Medical School for the past 29 years and continues to teach residents and medical students on a regular basis.[6]

Dr. Ticknor has treated hundreds of patients like Beth Forbes ("Mrs. Forbes") in his career with a diagnosis of bipolar disorder and/or severe, recurrent depressions.[7] In so doing, and unlike plaintiffs' experts, he has written or renewed thousands of prescriptions each year for medicines such as Depakote that are used to treat patients with bipolar disorders and depression.[8] He has also treated many women with bipolar disorder during their childbearing years and during their pregnancies.[9]

In addition to his clinical experience as a psychiatrist who has been practicing for 30 years – including the time during which Mrs. Forbes was prescribed Depakote to treat her bipolar

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[2] *See* Ex. 1, 6/26/15 Ticknor Exp. Rpt. at 1.
[3] *Id.*
[4] *Id.*
[5] *Id.*
[6] *Id.*
[7] *Id.* at 2.
[8] *Id.*
[9] *Id.*

disorder – Dr. Ticknor has reviewed research and publications on Depakote,[10] attended and participated in American Psychiatric Association meetings during which the birth defect risks of bipolar disorder treatment options such as Depakote were discussed,[11] and reviewed and interpreted the warnings in labeling of other drugs used to treat bipolar disorder and evaluated the comparative risk of birth defects.[12] He has also given numerous presentations concerning the evaluation, treatment, and long-term outcomes of patients with bipolar disorders and depression, and has published articles on depression.[13] Dr. Ticknor is therefore familiar with the data and science available to the medical community regarding Depakote's risk of birth defects and can address how psychiatrists such as Mrs. Forbes's prescribing physician and himself should evaluate those risks through the drug's label, literature, and other sources when making prescribing decisions for the treatment of bipolar disorder.

III. Dr. Ticknor Is Qualified To Offer An Opinion On The Adequacy Of Depakote's Birth Defect Warnings

Plaintiffs claim that Dr. Ticknor is not qualified to opine that the birth defect warnings in the Depakote label were adequate. They contend that because Dr. Ticknor lacks familiarity with the Food and Drug Administration ("FDA") rules and regulations applicable to pharmaceutical labeling and is not a "regulatory expert," he cannot offer opinions concerning the adequacy of the warnings in the Depakote label. (*See* pls.' memo. at 4-6, Doc. 151.) Plaintiffs' argument is meritless, particularly since the basic purpose of a label is for physicians such as Dr. Ticknor to

[10] *See* Ex. 2, 1/8/16 Ticknor Dep. at 34:22-35:11; *see also* Ex. 3, 4/15/16 Ticknor Dep. at 47:12-17.
[11] *See* Ex. 2, 1/8/16 Ticknor Dep. at 34:22-35:11; 52:6-53:2.
[12] *See* Ex. 2, 1/8/16 Ticknor Dep. at 48:2-49:13
[13] *See* Ex. 1, 6/26/15 Ticknor Exp. Rpt. at 2.

read and comprehend the warnings in it.[14] Moreover, plaintiffs do not – and cannot – point to any prohibition that renders doctors incapable of evaluating warning statements in a label. To the contrary, physicians are "fully qualified to opine on the medical facts and science regarding the risks and benefits of . . . drugs . . . and to compare that knowledge with what was provided in the text of labeling and warnings . . . ." *In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Prods. Liab. Litig.*, 2000 WL 876900, *11 (E.D. Pa. June 20, 2000).

Courts have repeatedly upheld this principle and recognized that physicians may offer opinions on the completeness and accurateness of the warning statements in a drug's label despite not being FDA or regulatory experts. Indeed, the U.S. District Court for the Southern District of Ohio recently reached this conclusion in *Rheinfrank v. Abbott Laboratories Inc.*, another Depakote case involving allegations of birth defects. In *Rheinfrank*, the court denied a motion to exclude a neurology expert without regulatory expertise from opining on the adequacy of Depakote's birth defect warnings, concluding that although the neurologist could not opine on regulatory aspects of the case, he could offer opinions on "the medical facts and science regarding the risks and benefits of Depakote and [could compare] that knowledge with what was provided in the text of the labeling." *Rheinfrank v. Abbott Labs. Inc.*, 119 F. Supp. 3d 749, 772-73 (S.D. Ohio 2015), reconsideration denied, 2015 WL 5836973 (S.D. Ohio Oct. 2, 2015); *see also In re Gadolinium-based Contrast Agents Prods. Liab. Litig.*, 2010 WL 1796334, *19 (N.D.

[14] Notably, plaintiffs' sole expert who will testify as to the adequacy of Depakote's birth defect warnings – Cheryl Blume – is not a physician, has never treated patients for bipolar disorder, and has never prescribed a single medicine. *See* Ex. 4, 2/28/14 Blume Dep. at 55:18-23; *see also* Ex. 5, 9/26/14 Blume Dep. at 78:10-22. Plaintiffs' position that Dr. Blume should be permitted to testify as to the Depakote warnings' adequacy but Dr. Ticknor should not is illogical, particularly since "Missouri courts have held that in cases involving manufacturers of prescription drugs, the manufacturer has a duty to properly warn the *doctor* of the dangers involved and it is incumbent upon the manufacturer *to bring the warning home to the doctor*." *In re Nuvaring Prods. Liab. Litig.*, 2013 WL 3716389, *5 (E.D. Mo. July 12, 2013) (internal quotations omitted) (emphasis in original and added).

Ohio May 4, 2010) (holding that a nephrologist who treated renally impaired patients was qualified to offer opinions on the adequacy of warning labels for gadolinium-based contrast agents based on his background as a physician, and his review of renal studies, published literature, and internal documents, even though he was not "a regulatory expert who has the expertise to opine on FDA regulations and the regulatory process . . . ."); *In re Diet Drugs*, 2000 WL 876900 at *11 (holding that physicians who admitted they were not "expert[s] in the regulatory field" were fully "qualified to render an opinion as to the labels' completeness, accuracy, and – it follows from that – the extent to which any inaccuracies or omissions could either deprive a reader or mislead a reader of what the risks and benefits of the . . . drugs in issue are or were at the time the labeling was published").[15] Glaringly absent from plaintiffs' motion is any authority that holds otherwise.

As explained in greater detail in section II above, Dr. Ticknor has evaluated Depakote as

[15] *See also In re Yasmin and Yaz (Drospirenone) Mktg., Sales Practices and Prods. Liab. Litig.*, 2011 WL 6301625, *11 (S.D. Ill. Dec. 16, 2011) (citing *In re Diet Drugs* with approval and holding that physician was "qualified to render an opinion as to the drug label's completeness and accurateness" without having "expertise in FDA regulations"); *In re Nuvaring Prods. Liab. Litig.*, 2013 WL 856218, *4 (E.D. Mo. Mar. 5, 2013) (denying defendants' motion to exclude the testimony of OB/GYNs or physiologist on the adequacy of Nuvaring's label because "none of the three possesses actual experience in the labeling of prescription drugs"); *In re Baycol Prods. Liab. Litig.*, 532 F. Supp. 2d 1029, 1063-64 (D. Minn. 2007) ("The Court agrees [with the holding in *In re Diet Drugs*] that [an expert who is a physician but not a regulatory expert] is qualified to render an opinion regarding the completeness or accuracy of the [] label based on his knowledge of the risks of [the drug] and his own clinical experience. He is not, however, qualified to render an opinion as to whether the [] labeling complied with FDA regulations."); *Mahaney v. Novartis Pharms. Corp.*, 2011 U.S. Dist. LEXIS 156848, *19 (W.D. Ky. Sept. 9, 2011) (holding that physician's "inexperience with the FDA labeling procedure" did not impact his "ability to review the relevant labels and give his opinion on whether they were sufficient to inform oncologists and other physicians about the risks of ONJ."); *Wilkerson v. Boston Sci. Corp.*, 2015 WL 2087048, *8 (S.D.W. Va. May 5, 2015) (urogynecologist "may testify about the risks he perceives that the product poses to patients and then opine that the [label] did not convey those risks" so long as he did not testify "as to what the product label should or should not have included under the law"); *Carlson v. Boston Sci. Corp.*, 2015 WL 1931311, *16 (S.D.W. Va. Apr. 28, 2015) (same).

a treatment option for mood disorders and prescribed it to hundreds of patients like Mrs. Forbes during his 30-year career as a psychiatrist.[16] In addition to his clinical experience and medical training, his review of research and literature,[17] attendance and participation at American Psychiatric Association meetings,[18] and review and interpretation of the warnings in labeling of other drugs used to treat bipolar disorder,[19] make him knowledgeable about the data and science known to the medical community regarding Depakote's risks and benefits. Dr. Ticknor is more than qualified, therefore, to render an opinion regarding the contents of the birth defect warnings in the Depakote label, including whether they provide adequate information to psychiatrists treating bipolar patients about the risk of birth defects, and this Court should permit him to do so.

IV. Dr. Ticknor Is Qualified To Opine On Depakote's Risk of Birth Defects

Despite plaintiffs' claim to the contrary, Dr. Ticknor is equally qualified to opine on Depakote's birth defect risk. Plaintiffs contend that Dr. Ticknor lacks experience, knowledge, or expertise about Depakote's risk of birth defects merely because, for example, he has not written any papers on the subject of birth defects or does not know how birth defect risk is assessed in regard to pharmaceutical drugs. (*See* pls.' memo. at 6-7.) Yet, plaintiffs ignore the undisputed facts that Dr. Ticknor:

- is knowledgeable about Depakote's risk of birth defects through his medical schooling, residency training, and 30-year career as a physician;[20]
- has reviewed literature and research on Depakote, including publications concerning Depakote's risk of birth defects;[21]

[16] *See* Ex. 2, 1/8/16 Ticknor Dep. at 59:3-16.
[17] *See* Ex. 2, 1/8/16 Ticknor Dep. at 34:22-35:11; *see also* Ex. 3, 4/15/16 Ticknor Dep. at 47:12-17.
[18] *See* Ex. 2, 1/8/16 Ticknor Dep. at 34:22-35:11; 52:6-53:2.
[19] *See* Ex. 2, 1/8/16 Ticknor Dep. at 48:2-49:13
[20] *See* Ex. 3, 4/15/16 Ticknor Dep at 45:24-46:12; 82:7-83:3.
[21] *See* Ex. 2, 1/8/16 Ticknor Dep. at 34:22-35:11; *see also* Ex. 3, 4/15/16 Ticknor Dep. at 47:12-17.

- has attended and participated in meetings of the American Psychiatric Association during which the birth defect risks of bipolar disorder treatment options, including Depakote, have been discussed;[22]

- has reviewed the warning labeling of drugs that are used to treat bipolar disorder, including Lithium, Lamictal, Depakote, and Tegretol, and evaluated the comparative incidence of neural tube defects;[23]

- has treated many women with bipolar disorder during their childbearing years and during their pregnancies;[24] and

- has prescribed Depakote for hundreds of patients, including women of childbearing age.[25]

Given his medical knowledge, training, and experience evaluating bipolar treatment options like Depakote, Dr. Ticknor is clearly qualified to opine on the science and medical facts surrounding Depakote's birth defect risk and how psychiatrists such as himself should consider those risks when making prescribing decisions for the treatment of bipolar disorder.[26]

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[22] *See* Ex. 2, 1/8/16 Ticknor Dep. at 34:22-35:11; 52:6-53:2.
[23] *See* Ex. 2, 1/8/16 Ticknor Dep. at 48:2-49:13
[24] *See* Ex. 1, 6/26/15 Ticknor Exp. Rpt. at 2.
[25] *See* Ex. 2, 1/8/16 Ticknor Dep. at 34:22-35:11; *see also* Ex. 6, 7/7/14 Ticknor Dep. at 35:25-36:8.
[26] Notably, while plaintiffs object to Dr. Ticknor's opinion concerning Depakote's risk of birth defects, they simultaneously seek to have Dr. Cheryl Blume provide this opinion. *See, e.g.*, Ex. 7, 1/26/15 Blume Declaration at ¶ 116 ("The literature continued to note that Depakene/Depakote treatment had a greater risk than other AEDs [antiepileptic drugs] of being associated with major congenital malformations, and that the association was considered causal and linked to increased treatment doses during pregnancy"); *id.* at ¶ 120 ("The risk of fetal exposure to both VPA monotherapy and polytherapy and the congenital malformation of spina bifida was found to be causally related to VPA exposure again in the early 1990s"). As stated above, Dr. Blume is not doctor, has never treated patients for bipolar disorder, and has never prescribed a pharmaceutical drug. *See* Ex. 4, 2/28/14 Blume Dep. at 55:18-23; *see also* Ex. 5, 9/26/14 Blume Dep. at 78:10-22. In addition, she has not published anything on birth defects and she has not been involved in the evaluation of a cause of a birth defect in a child. *See* Ex. 4, 2/28/14 Blume Dep. at 58:18-20; 60:1-4. Nor has she spoken with any other doctor, M.D. or Ph.D., about Depakote's risk of birth defects. *See* Ex. 5, 9/26/14 Blume Dep. at 87:10-13. Plaintiffs' own expert designation, therefore, contradicts their argument that Dr. Ticknor should be prohibited from opining on Depakote's birth defect risk.

V. Permitting Dr. Ticknor To Offer Opinions On The Adequacy Of Depakote's Birth Defect Warnings And Depakote's Risk Of Birth Defects Would Not Cause Plaintiffs Substantial Prejudice, Would Not Cause Confusion, And Would Not Be Cumulative Evidence

Plaintiffs baldly conclude in their motion that Dr. Ticknor's opinions on the adequacy of Depakote's warnings and Depakote's birth defect risk should be excluded because they "would be highly prejudicial and confusing." (*See* pls.' memo. at 7, Doc. 151.) Under Rule 403, "[u]nfair prejudice . . . means an undue tendency to suggest decision on an improper basis, commonly, though not necessarily, an emotional one." *Cummings v. Malone*, 995 F.2d 817, 824 (8th Cir. 1993) (quoting Fed. R. Evid. 403 advisory committee's note); *see also McEwen v. City of Norman, Okl.*, 926 F.2d 1539, 1549-50 (10th Cir. 1991) (stating that unfair prejudice "cannot be equated with testimony which is simply unfavorable to a party. It must be unfair in the sense that it would be misleading and not aid and assist the jury in making a material determination in the case."). "The burden under Rule 403 is on the party opposing admission, who must show that the probative value 'is *substantially outweighed* by the danger of *unfair prejudice*'." *U.S. v. Tse*, 375 F.3d 148, 164 (1st Cir. 2004) (emphasis in original). Nowhere in plaintiffs' motion do they include any explanation as to how Dr. Ticknor's opinions would unfairly prejudice them. As such, their argument fails. *See Burlington N. and Santa Fe Ry. Co. v. Bellefontaine Quarry Inc.*, 2002 WL 34354484, *3 (E.D. Mo. July 1, 2002) (denying defendant's motion to exclude expert's testimony because defendant did not show "the degree of unfair surprise or prejudice necessary to exclude" the expert's testimony).

Plaintiffs' claim that Dr. Ticknor's opinions would be cumulative is equally without merit. In making this argument, plaintiffs inappropriately obfuscate Dr. Ticknor's opinions with those of Abbott's regulatory expert, Dr. Karen Becker ("Dr. Becker"), and Abbott's medical causation expert, Dr. John Graham ("Dr. Graham"). Dr. Becker, a pharmacologist with over 30

years of regulatory experience concerning the product development process and the complex requirements for marketing authorization of drugs and medical devices by the FDA, will opine on the Depakote label's compliance with applicable FDA rules, regulations, guidance, and policy, including the adequacy of Depakote's birth defect warnings as measured by FDA standards. (*See* Pls.' Ex. A, Becker Exp. Rpt., Doc. 151-1.) In contrast, Dr. Graham, a board-certified pediatrician and medical geneticist with over 35 years of training and experience in clinical genetics, dysmorphology, birth defects, developmental disabilities, communicative disorders, and public health aspects of birth defects, will not offer an opinion on the adequacy of the birth defect warnings in the Depakote label, but will instead opine on the general science of birth defects and the cause of B.F's spina bifida. (*See* Ex. 8, 6/26/15 Graham Exp. Rpt. at ¶ 12.) Finally, and as explained above, Dr. Ticknor, as a clinical psychiatrist in his 30th year of practice and who regularly prescribes medication for patients suffering from bipolar disorder, will opine as to the medical data and science regarding the birth defect risk of Depakote known to the medical community and whether the birth defect warnings in the Depakote label contained adequate information to inform physicians like himself who treat bipolar patients about the birth defect risk associated with administration of Depakote.

None of these opinions is cumulative of another. Indeed, each provides a unique perspective and addresses a specific and independent underlying issue in this litigation: regulatory compliance, medical causation, and interpretation of the completeness and accurateness of Depakote's warnings by prescribing physicians. *See Spartan, L.L.C. v. Kansas City Title, Inc.*, 2008 WL 5500912, *1-3 (W.D. Mo. July 29, 2008) (denying defendants' motion to exclude expert's testimony as unfairly redundant and duplicative of a second expert's after recognizing that "[t]here are many kinds of experts and many kinds of expertise that are

recognized by the law" and the experts "[we]re testifying from different perspectives and ha[d] different qualifications"); *Kay v. Lamar Advert. of S. Dakota, Inc.*, 2009 WL 2525204, *2 (D.S.D. Aug. 17, 2009) (denying defendants' motion to limit plaintiffs' ability to call more than one accident reconstruction expert at trial because defendants did not show "the testimony to be a '*needless* presentation of cumulative evidence'," and the experts' testimony pertained to the underlying, and not ancillary, issues before the court). Even assuming, however, that there is overlap between Dr. Ticknor's and Dr. Becker's opinions concerning the adequacy of Depakote's birth defect warnings, Abbott would be willing to withdraw Dr. Becker from testifying on any point on which her testimony overlaps with Dr. Ticknor's and/or take any other necessary steps to ensure that the two experts' testimony is not repetitive or cumulative.[27]

CONCLUSION

For all of the foregoing reasons, plaintiffs' motion *in limine* no. 6 should be denied.

Date: May 5, 2016

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[27] For example, Abbott could perceive a situation in which, after Dr. Ticknor's testimony and Abbott's cross-examination of plaintiffs' regulatory expert, Dr. Becker would no longer be a necessary witness and Abbott would forego calling her to testify at trial.

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on May 5, 2016, the foregoing was filed electronically with the Clerk of Court to be served by operation of the Court's electronic filing system on all counsel of record.

/s/ Dan H. Ball